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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/566,068

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EXAMINER

YOUNG, SHAWQUA

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/566,068	Applicant(s) BIRCH ET AL.	
	Examiner SHAWQUIA YOUNG	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-10 and 16-22 is/are pending in the application.
- 4a) Of the above claim(s) 16 and 20-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-10,17 and 18 is/are rejected.
- 7) ☒ Claim(s) 19 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1, 3-10 and 16-22 are currently pending in the instant application. Claims 1, 3-10, 17 and 18 are being rejected, claim 19 is being objected and claims 16 and 20-22 are withdrawn from consideration in this Office Action.

I. ***Response to Arguments/Remarks***

Applicants, amendment filed on January 12, 2009, has overcome the rejection of claim 19 under 35 USC 112, second paragraph as being incomplete for omitting essential structural cooperative relationships of elements. The above rejection has been withdrawn.

Applicant's arguments with respect to the rejection of claims 1, 3-10, 17 and 18 under 35 USC 103 as being unpatentable over Strobel, et al. (US 2003/0055093) have been fully considered but are not persuasive. Applicants argue that the indanyl amide portion of the molecule bears a specific substituent namely an optionally substituted indole-2-yl group. Applicants further argue that although indole is included within the definition of Heter groups allowed in the variables recited for the group at the corresponding position in the molecule R⁵ in the compound of Strobel, that the average skilled man would have no reason to select B as CH-(C₁₋₃alkyl) and R⁵ as indole in combination based on the disclosure. Applicants also argue that although Strobel provides examples of compound in which indolyl, these are very few in number compared to the well over four hundred compounds in total exemplified Strobel.

However, the Examiner wants to point out that the options for variable B is not a long laundry list of possibilities. The definition of variable B is very limited and thus it would be obvious for one of ordinary skill in the art to make a similar compound to an example in Strobel, et al. such as 5-bromo-1H-indole-2-carboxylic acid indan-2ylamide (See ex 241, page 30) wherein B is CH-(C₁₋₃ alkyl) with a reasonable expectation of success. The motivation for one of ordinary skill in the art to prepare a similar compound but to modify the variable would be it has been well established that substituting a hydrogen with a methyl is considered obvious because these two functional groups are considered obvious variants. The Examiner wants to also point out that the number of compounds that contain an indole group that have been disclosed in the Strobel, et al. reference in relation to the other types of compounds is irrelevant. The prior art specifically teaches examples of compounds wherein R⁵ is indole which means that these types of compounds were developed and studied. The prior art is not limited to the examples or preferred embodiments and therefore it would be obvious for one of ordinary skill in the art to modify, for example, 5-bromo-1H-indole-2-carboxylic acid indan-2ylamide wherein B is CH-(C₁₋₃ alkyl) and expect the compound to possess activity. Applicants have failed to persuasively argue that the instant compounds wherein Y is alkyl are not obvious over the prior art reference, Strobel, et al. Thus the Examiner has maintained the obviousness rejection of claims 1, 3-10, 17 and 18 as being unpatentable over *Strobel, et al.*

II. **Rejection(s)**

35 USC § 103 - OBVIOUSNESS REJECTION

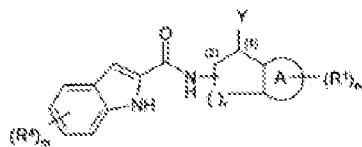
The following is a quotation of 35 U.S.C. § 103(a) that forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Graham v. John Deere Co. set forth the factual inquiries necessary to determine obviousness under 35 U.S.C. § 103(a). See *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Specifically, the analysis must employ the following factual inquiries:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3-10, 17 and 18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over *Strobel, et al.* (US 2003/0055093). Applicants claim a compound of

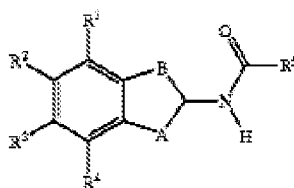


formula

wherein all variables are as defined in claim 1.

The Scope and Content of the Prior Art (MPEP §2141.01)

Strobel, et al. teaches acylated indanyl amines that are useful in the upregulation of endothelial nitric oxide synthase (eNOS). The invention is represented by the general formula:



[0012] In the above formula,

[0013] R^1 and R^4 are independently from each other selected from the group consisting of:

[0014] H; unsubstituted and at least monosubstituted C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl and C_3 - C_{10} -alkynyl, the substituents of which are selected from the group consisting of F, OH, C_1 - C_3 -alkoxy, $(C_1$ - C_6 -alkyl)mercapto, CN, $COOR^5$, $CONR^5$, and unsubstituted and at least monosubstituted phenyl and heteroaryl, the substituents of which are selected from the group consisting of halogens, pseudohalogens, C_1 - C_3 -alkyl, C_1 - C_3 -alkoxy and CF_3 ; unsubstituted and at least monosubstituted phenyl and heteroaryl, the substituents of which are selected from the group consisting of halogens, pseudohalogens, C_1 - C_3 -alkyl, C_1 - C_3 -alkoxy and CF_3 ; R^5CO , $CONR^{13}R^{11}$, $COOR^{12}$, CF_3 ; halogens; pseudohalogens; $NR^{13}R^{14}OR^{15}$, $S(O)_mR^{16}$, $SO_2NR^{17}R^{18}$; and NO_2 ;

[0015] R^2 and R^3 are independently from each other selected from the group consisting of:

[0016] H; halogens; pseudohalogens; unsubstituted and at least monosubstituted C_1 - C_{10} -alkyl the substituents of which are selected from the group consisting of OH, phenyl, and heteroaryl; OH; C_1 - C_{10} -alkoxy; phenoxy; $S(O)_mR^{19}$; CF_3 ; CN; NO_2 ; $(C_1$ - C_{10} -alkyl)amino; $di(C_1$ - C_{10} -alkyl)amino $(C_1$ - C_6 -alkyl)-CONH—; unsubstituted and at least monosubstituted phenyl-CONH— and phenyl- SO_2 —O—, the substituents of which are selected from the group consisting of halogens, pseudohalogens, CH_3 and methoxy; $(C_1$ - C_6 -alkyl) SO_2 —O—; unsubstituted and at least monosubstituted $(C_1$ - C_6 -alkyl)CO, the substituents of which are selected from the group consisting of F, $di(C_1$ - C_3 -alkyl)amino, pyrrolidinyl and piperidinyl; and phenyl-CO, the phenyl part of which can be substituted by one or more substituents from the group consisting of C_1 - C_3 -alkyl, halogens and methoxy;

[0017] A is selected from the group consisting of CH_2 , $CHOH$ and CH —(C_1 - C_3 -alkyl);

[0018] B is selected from the group consisting of CH_2 and CH —(C_1 - C_3 -alkyl);

[0019] R^5 is a group Ar or a group Hetar both of which can be unsubstituted or carry one or more substituents selected from the group consisting of: halogens; pseudohalogens; NH_2 ; unsubstituted and at least monosubstituted C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl, C_3 - C_{10} -alkynyl, C_2 - C_{10} -alkoxy, $(C_1$ - C_{10} -alkyl) amino, $di(C_1$ - C_{10} -alkyl)amino, the substituents of which are selected from the group consisting of F, OH, C_1 - C_3 -alkoxy, aryloxy, $(C_1$ - C_6 -alkyl)mercapto, NH_2 , $(C_1$ - C_6 -alkyl)amino, and $di(C_1$ - C_6 -alkyl) amino; C_3 - C_5 -alkandyl; phenyl; heteroaryl; aryl- or heteroaryl-substituted C_2 - C_4 -alkyl; CF_3 ; NO_2 ; OH; phenoxy; benzyloxy; $(C_1$ - C_{10} -alkyl)COO; $S(O)_mR^{20}$; SH; phenylamino; benzylamino; $(C_1$ - C_{10} -alkyl)-CONH—; $(C_1$ - C_{10} -alkyl)-CON(C_1 - C_6 -alkyl); phenyl-CONH—; phenyl-CON(C_1 - C_6 -alkyl); heteroaryl-CONH—; heteroaryl-CON(C_1 -

C_6 -alkyl); $(C_1$ - C_{10} -alkyl)-CO; phenyl-CO; heteroaryl-CO; CF_3 -CO; —OCH₂O—; —OCF₃O—; —OCH₂CH₂O—; —CH₂CH₂O—; $COOR^{21}$, $CONR^{22}R^{23}$, $CNH(NH_2)$, $SO_2NR^{24}R^{25}$, $R^{26}SO_2NH$ —, $R^{27}SO_2N(C_1$ - C_6 -alkyl)—; and saturated or at least monounsaturated aliphatic, mononuclear 5- to 7-membered heterocycles containing 1 to 3 heteroatoms selected from the group consisting of N, O and S, which heterocycles can be substituted by one or more substituents selected from the group consisting of halogens, C_1 - C_3 -alkyl, C_1 - C_3 -alkoxy, OH, oxo and CF_3 , where said heterocycles can optionally be condensed to the said group Ar or the said group Hetar; wherein all aryl, heteroaryl, phenyl, aryl-containing, heteroaryl-containing and phenyl-containing groups, which are optionally present in the said substituents of the said group Ar or the said group Hetar, can be substituted by one or more substituents selected from the group consisting of halogens, pseudohalogens, C_1 - C_3 -alkyl, OH, C_1 - C_3 -alkoxy, and CF_3 ;

[0020] R^6 is selected from the group consisting of:

[0021] H; C_1 - C_{10} -alkyl, which can be substituted by one or more substituents selected from the group consisting of F, C_1 - C_6 -alkoxy, and $di(C_1$ - C_6 -alkyl)amino; aryl- $(C_1$ - C_6 -alkyl) and heteroaryl- $(C_1$ - C_6 -alkyl), which can be substituted by one or more substituents selected from the group consisting of halogens, C_1 - C_4 -alkoxy, and $di(C_1$ - C_6 -alkyl)amino;

[0022] R^7 is selected from the group consisting of:

[0023] H; C_1 - C_{10} -alkyl which can be substituted by one or more substituents selected from the group consisting of F, C_1 - C_6 -alkoxy, $di(C_1$ - C_6 -alkyl)amino and phenyl; phenyl; indanyl; and heteroaryl; and wherein each of the aforementioned aromatic groups can be unsubstituted or carry one or more substituents from the group consisting of halogens, pseudohalogens, C_1 - C_3 -alkyl, C_1 - C_3 -alkoxy and CF_3 ;

[0024] R^8 is H or C_1 - C_{10} -alkyl;

[0025] R^9 is selected from the group consisting of: C_1 - C_{10} -alkyl which can be unsubstituted or carry one or more substituents from the group consisting of: F, $(C_1$ - C_6 -alkoxy, $di(C_1$ - C_6 -alkyl)amino; and unsubstituted and at least monosubstituted phenyl and heteroaryl, the substituents of which are selected from the group consisting of C_1 - C_3 -alkyl, C_1 - C_3 -alkoxy, halogens, pseudohalogens, and CF_3 ;

[0026] R^{10} independently has the same meaning as R^7 ;

[0027] R^{11} independently has the same meaning as R^8 ;

[0028] R^{12} independently has the same meaning as R^9 ;

[0029] R^{13} is selected from the group consisting of: H; C_1 - C_6 -alkyl; unsubstituted and substituted phenyl, benzyl, heteroaryl, $(C_1$ - C_6 -alkyl)-CO, phenyl-

wherein specifically r is 1 and Y can represent an optionally substituted (1-4C)alkyl. The prior art reference of *Strobel, et al.* teaches a similar compound wherein the variable of B (equivalent to the CH-Y in the instant application) can be CH₂ or CH-(C₁-C₃-alkyl) (See page 2, paragraph 0018). The prior art reference also teaches specific compounds such as 5-bromo-1H-indole-2-carboxylic acid indan-2-ylamide (See ex 241, page 30), 7-nitro-1H-indole-2-carboxylic acid indan-2-ylamide (See ex 252, page 31), 5-methyl-1H-indole-2-carboxylic acid indan-2-ylamide (See ex 254, page 31), etc.

In Ex parte Bluestone, 135 USPQ 199, it was well established that the interchange of alkyl and hydrogen is obvious in and of itself. For example, it is obvious to prepare an alkyl substituted (i.e. methyl) indanyl amine derivative wherein the indanyl ring is substituted at carbon 1 when the art teaches an unsubstituted acylated indanylamine wherein the indanyl ring could be substituted at carbon 1 with a C₁-C₃ alkyl with a reasonable expectation of success. Specifically, a methylsubstituted indanyl ring and an unsubstituted indanyl ring are considered homologues and are obvious absent unexpected results. Therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to prepare adjacent homologs based on the teachings of the preferred embodiments in the prior art. A strong prima facie obviousness has been established.

III. ***Objection***

Dependent Claim Objections

Dependent Claim 19 is objected to as being dependent upon a rejected based claim. To overcome this objection, Applicant should rewrite said claim in an independent form and include the limitations of the base claim and any intervening claim.

IV. ***Conclusion***

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 7:00 AM-3:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

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For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shawquia Young/

Examiner, Art Unit 1626

/Rebecca L Anderson/

Primary Examiner, Art Unit 1626